FIG. 1A

TCTAGATCTA GCTGGTGTGT CTCTGATCTT GCTTCTTTTC TCCCAGCCCT 50

TCCTACTTGT GTGAGAACAA GGTTTTGAGC CATGGAGCAA AGAGGTTGGA 100

CTCTGCAGTG TACTGCTTTC GCCTTCTTTT GCGTTTGGTG TGCACTAAGC 150

AGTGTAAAAG CAAAGAGGCA GTTTGTTAAT GAATGGGCGG CGGAGATCCC 200

CGGAGGGCAA GAAGCTGCCT CTGCCATCGC CGAAGAACTG GGGTATGACC 250

TTTTGGGTCA GATTGGATCA CTTGAAAATC ACTATTTATT CAAACACAAA 300

AGCCATCCTC GGAGGTCCCG AAGAAGCGCT CTTCATATCA CTAAGAGGTT 350

ATCTGATGAT GATCGTGTGA CGTGGGCTGA ACAACAGTAT GAAAAAGAGA 400

GAAGTAAACG TTCAGTTCAA AAAGACTCAG CATTGGATCT CTTCAATGAT 450

CCAATGTGGA ATCAGCAGTG GTACTTGCAA GATACCAGAA TGACTGCAGC 500

TCTGCCCAAG CTGGACCTTC ATGTAATACC TGTTTGGGAA AAGGGTATTA 550

CTGGCAAAGG AGTTGTTATT ACTGTACTGG ATGATGGCTT GGAGTGGAAT 600

CACACAGACA TTTATGCCAA TTATGATCCA GAGGCTAGCT ATGATTTTAA 650

CGATAATGAT CATGATCCAT TTCCCCGATA TGATCTCACA AATGAAAACA 700

AACATGGAAC AAGATGTGCA GGTGAAATTG CCATGCAAGC AAATAATCAC 750

AAGTGTGGGG TTGGAGTTGC ATATAATTCC AAAGTTGGAG GCATAAGAAT 800

FIG. IB

GCTGGATGGC ATTGTAACTG ATGCCATTGA GGCTAGTTCA ATTGGATTCA 850

ACCCTGGCCA TGTGGATATT TACAGTGCAA GCTGGGGCCC TAATGATGAT 900

GGAAAAACTG TGGAGGGGCC TGGCAGACTA GCCCAGAAGG CATTTGAATA 950

TGGTGTCAAA CAGGGGAGAC AAGGGAAAGG CTCCATCTTT GTCTGGGCTT 1000

CAGGGAATGG GGGTCGTCAG GGAGATAACT GTGACTGTGA TGGCTACACA 1050

GACAGCATTT ACACCATCTC TATCAGCAGT GCCTCCCAGC AAGGCCTGTC 1100

ACCTTGGTAT GCAGAGAAGT GTTCTTCCAC ATTGGCTACC TCCTACAGCA 1150

GTGGTGATTA CACAGACCAG CGAATAACAA GCGCTGACCT GCACAATGAC 1200

TGCACAGAGA CCCACACAGG CACCTCGGCT TCAGCACCCC TGGCTGCTGG 1250

TATCTTTGCT CTGGCCTTGG AGGCAAACCC AAATCTTACC TGGAGAGATA 1300

TGCAGCATCT GGTTGTCTGG ACCTCTGAGT ACGACCCATT GGCCAGTAAC 1350

CCAGGTTGGA AAAAGAATGG GGCAGGCTTG ATGGTGAACA GCCGATTTGG 1400

ATTTGGCTTG CTAAATGCCA AAGCTCTGGT GGATTTGGCT GATCCTCGGA 1450

CCTGGAGAAA TGTGCCTGAG AAGAAAGAAT GTGTTGTAAA AGACAATAAC 1500

TTTGAGCCTA GAGCCCTGAA AGCTAATGGA GAAGTAATTG TTGAAATCCC 1550

AACAAGAGCT TGTGAAGGAC AAGAAAATGC TATCAAGTCT CTGGAACATG 1600

TGCAATTTGA AGCAACAATT GAATATTCTC GTAGAGGAGA CCTTCATGTC 1650

FIG. IC

ACACTCACTT CTGCTGTTGG AACCAGCACT GTACTGTTGG CTGAAAGGGA 1700

AAGAGATACA TCCCCCAATG GCTTTAAGAA TTGGGACTTC ATGTCTGTTC 1750

ATACATGGGG AGAGAATCCT GTAGGCACCT GGACATTGAA AATTACAGAC 1800

ATGTCTGGAA GAATGCAAAA TGAAGGAAGG ATTGTGAACT GGAAGTTGAT 1850

TTTGCATGGG ACATCTTCTC AACCAGAGCA CATGAAGCAG CCCCGTGTGT 1900

ACACATCCTA CAATACAGTC CAGAATGACA GGAGAGGAGT GGAAAAGATG 1950

CCTGGTACCC AAAAACTCCA GCAGCAGCAA TGTGGAGGGT AGAAGGGATG 2050

AGCAGGTACA AGGAACTCCT TCAAAGGCCA TGCTGCGACT CCTACAAAGT 2100

GCTTTTAGCA AGAATGCACT TTCAAAACAA TCACCAAAGA AGTCTCCAAG 2150

TGCAAAGCTC AGCATCCCTT ATGAAAGTTT CTATGAAGCC TTGGAAAAGC 2200

TTAACAAGCC CTCCAAGCTT GAAGGCTCTG AAGACAGTCT GTACAGTGAC 2250

TATGTTGATG TATTCTATAA CACAAAACCT TATAAGCATA GAGATGACAG 2300

GCTGCTGCAA GCTCTCATGG ACATCCTAAA TGAGGAGAAT TAAAATAAGG 2350

AGCTC 2355

FIG. 2A

TCTAGATGCA TCTTCCCTCT TCGTCCCCTG CTCCACCACC CTGCGCGCCT 50

CACAGCCCCG CTTTTCACTC CCAAAGAAGG ATGGAGGGCG GTTGTGGATC 100

CCAGTGGAAG GCGGCCGGGT TCCTCTTCTG TGTGATGGTT TTTGCGTCTG 150

CCGAGAGACC CGTCTTCACG AATCATTTTC TTGTGGAGTT GCATAAAGAC 200

GGAGAGGAAG AGGCTCGCCA AGTTGCAGCA GAACACGGCT TTGGAGTCCG 250

AAAGCTCCCC TTTGCAGAAG GCCTGTATCA CTTTTATCAC AATGGGCTTG 300

CAAAGGCCAA AAGAAGACGC AGCCTACACC ATAAGCGGCA GCTAGAGAGA 350

GACCCCAGGA TAAAGATGGC GCTGCAACAA GAAGGATTTG ACCGTAAAAA 400

GAGAGGGTAC AGGGACATCA ATGAGATTGA CATCAACATG AATGATCCTC 450

TCTTTACAAA GCAATGGTAC CTGTTCAACA CTGGGCAAGC CGATGGAACT 500

CCTGGGCTAG ACTTGAACGT GGCCGAAGCC TGGGAGCTGG GATACACAGG 550

AAAAGGAGTG ACCATTGGAA TTATGGATGA TGGAATTGAC TATCTCCACC 600

CAGACCTGGC CTACAACTAC AACGCTGATG CAAGTTATGA CTTCAGCAGC 650

AATGACCCCT ACCCATACCC TCGATACACA GATGACTGGT TCAACAGCCA 700

TGGAACTAGG TGTGCAGGAG AAGTTTCTGC TGCAGCCAGC AACAATATCT 750

GTGGAGTCGG CGTAGCATAC AACTCCAAGG TGGCAGGGAT CCGGATGCTG 800

GACCAGCCCT TTATGACAGA CATCATCGAA GCCTCCTCCA TCAGCCACAT 850

FIG. 2B

GCCTCAACTG ATCGACATCT ACAGTGCAAG CTGGGGCCCC ACAGACAATG 900

GGAAGACGGT TGATGGGCCC CGAGAGCTCA CACTCCAGGC CATGGCTGAT 950

GGCGTGAACA AGGGCCGTGG GGGCAAAGGC AGCATCTATG TGTGGGCCTC 1000

TGGGGACGGT GGCAGCTACG ATGACTGCAA CTGTGACGGC TATGCTTCAA 1050

GCATGTGGAC CATCTCCATC AACTCAGCCA TCAATGATGG CAGGACTGCC 1100

TTGTATGATG AGAGTTGCTC TTCCACCTTA GCATCCACCT TCAGCAATGG 1150

GAGGAAGAGG AATCCTGAGG CTGGTGTGGC TACCACAGAC TTGTATGGCA 1200

ACTGTACTCT GAGACACTCT GGGACATCTG CAGCTGCTCC GGAGGCAGCT 1250

GGCGTGTTTG CATTAGCTTT GGAGGCTAAC CTGGATCTGA CCTGGAGAGA 1300

CATGCAACAT CTGACTGTGC TCACCTCCAA GCGGAACCAG CTTCATGATG 1350

AGGTTCATCA GTGGCGACGG AATGGGGTTG GCCTGGAATT TAATCACCTC 1400

TTTGGCTACG GAGTCCTTGA TGCAGGTGCC ATGGTGAAAA TGGCTAAAGA 1450

CTGGAAAACT GTTCCGGAGA GATTCCATTG TGTGGGAGGC TCTGTGCAGA 1500

ACCCTGAAAA AATACCACCC ACCGGCAAGC TGGTACTGAC CCTCAAAACA 1550

AATGCATGTG AGGGGAAGGA AAACTTCGTC CGCTACCTGG AGCACGTCCA 1600

AGCTGTCATC ACAGTCAACG CGACCAGGAG AGGAGACCTG AACATCAACA 1650

FIG. 2C

```
TGACCTCCCC AATGGGCACC AAGTCCATTT TGCTGAGCCG GCGTCCCAGA 1700

GACGACGACT CCAAGGTGGG CTTTGACAAG TGGCCTTTCA TGACCACCCA 1750

CACCTGGGGG GAGGATGCCC GAGGGACCTG GACCCTGGAG CTGGGGTTTG 1800

TGGGCAGTGC ACCACAGAAG GGGTTGCTGA AGGAATGGAC CCTGATGCTT 1850

CACGGCACAC AGAGCGCCCC ATACATCGAT CAGGTGGTGA GGGATTACCA 1900

GTCTAAGCTG GCCATGTCCA AGAAGCAGGA GCTGGAGGAA GAGCTGGATG 1950

AGGCTGTGGA GAGAAGCCTG CAAAGTATCC TGAGAAAGAA CTAGGGCCAC 2000

GCTTCCGAAT TC 2012
```

FIG. 3A

```
Met Glu Gln Arg Gly Trp Thr Leu Gln Cys Thr Ala Phe Ala Phe
  1               5                  10                  15

Phe Cys Val Trp Cys Ala Leu Ser Ser Val Lys Ala Lys Arg Gln
             20                  25                  30

Phe Val Asn Glu Trp Ala Ala Glu Ile Pro Gly Gly Gln Glu Ala
             35                  40                  45

Ala Ser Ala Ile Ala Glu Glu Leu Gly Tyr Asp Leu Leu Gly Gln
             50                  55                  60

Ile Gly Ser Leu Glu Asn His Tyr Leu Phe Lys His Lys Ser His
             65                  70                  75

Pro Arg Arg Ser Arg Arg Ser Ala Leu His Ile Thr Lys Arg Leu
             80                  85                  90

Ser Asp Asp Asp Arg Val Thr Trp Ala Glu Gln Gln Tyr Glu Lys
             95                  100                 105

Glu Arg Ser Lys Arg Ser Val Gln Lys Asp Ser Ala Leu Asp Leu
            110                 115                 120

Phe Asn Asp Pro Met Trp Asn Gln Gln Trp Tyr Leu Gln Asp Thr
            125                 130                 135

Arg Met Thr Ala Ala Leu Pro Lys Leu Asp Leu His Val Ile Pro
            140                 145                 150

Val Trp Glu Lys Gly Ile Thr Gly Lys Gly Val Val Ile Thr Val
            155                 160                 165

Leu Asp Asp Gly Leu Glu Trp Asn His Thr Asp Ile Tyr Ala Asn
            170                 175                 180

Tyr Asp Pro Glu Ala Ser Tyr Asp Phe Asn Asp Asn Asp His Asp
            185                 190                 195

Pro Phe Pro Arg Tyr Asp Leu Thr Asn Glu Asn Lys His Gly Thr
            200                 205                 210

Arg Cys Ala Gly Glu Ile Ala Met Gln Ala Asn Asn His Lys Cys
            215                 220                 225

Gly Val Gly Val Ala Tyr Asn Ser Lys Val Gly Gly Ile Arg Met
            230                 235                 240
```

FIG. 3B

```
Leu Asp Gly Ile Val Thr Asp Ala Ile Glu Ala Ser Ser Ile Gly
                245                 250                 255

Phe Asn Pro Gly His Val Asp Ile Tyr Ser Ala Ser Trp Gly Pro
                260                 265                 270

Asn Asp Asp Gly Lys Thr Val Glu Gly Pro Gly Arg Leu Ala Gln
                275                 280                 285

Lys Ala Phe Glu Tyr Gly Val Lys Gln Gly Arg Gln Gly Lys Gly
                290                 295                 300

Ser Ile Phe Val Trp Ala Ser Gly Asn Gly Gly Arg Gln Gly Asp
                305                 310                 315

Asn Cys Asp Cys Asp Gly Tyr Thr Asp Ser Ile Tyr Thr Ile Ser
                320                 325                 330

Ile Ser Ser Ala Ser Gln Gln Gly Leu Ser Pro Trp Tyr Ala Glu
                335                 340                 345

Lys Cys Ser Ser Thr Leu Ala Thr Ser Tyr Ser Ser Gly Asp Tyr
                350                 355                 360

Thr Asp Gln Arg Ile Thr Ser Ala Asp Leu His Asn Asp Cys Thr
                365                 370                 375

Glu Thr His Thr Gly Thr Ser Ala Ser Ala Pro Leu Ala Ala Gly
                380                 385                 390

Ile Phe Ala Leu Ala Leu Glu Ala Asn Pro Asn Leu Thr Trp Arg
                395                 400                 405

Asp Met Gln His Leu Val Val Trp Thr Ser Glu Tyr Asp Pro Leu
                410                 415                 420

Ala Ser Asn Pro Gly Trp Lys Lys Asn Gly Ala Gly Leu Met Val
                425                 430                 435

Asn Ser Arg Phe Gly Phe Gly Leu Leu Asn Ala Lys Ala Leu Val
                440                 445                 450

Asp Leu Ala Asp Pro Arg Thr Trp Arg Asn Val Pro Glu Lys Lys
                455                 460                 465

Glu Cys Val Val Lys Asp Asn Asn Phe Glu Pro Arg Ala Leu Lys
                470                 475                 480
```

FIG. 3C

```
Ala Asn Gly Glu Val Ile Val Glu Ile Pro Thr Arg Ala Cys Glu
                485                 490                 495

Gly Gln Glu Asn Ala Ile Lys Ser Leu Glu His Val Gln Phe Glu
                500                 505                 510

Ala Thr Ile Glu Tyr Ser Arg Arg Gly Asp Leu His Val Thr Leu
                515                 520                 525

Thr Ser Ala Val Gly Thr Ser Thr Val Leu Leu Ala Glu Arg Glu
                530                 535                 540

Arg Asp Thr Ser Pro Asn Gly Phe Lys Asn Trp Asp Phe Met Ser
                545                 550                 555

Val His Thr Trp Gly Glu Asn Pro Val Gly Thr Trp Thr Leu Lys
                560                 565                 570

Ile Thr Asp Met Ser Gly Arg Met Gln Asn Glu Gly Arg Ile Val
                575                 580                 585

Asn Trp Lys Leu Ile Leu His Gly Thr Ser Ser Gln Pro Glu His
                590                 595                 600

Met Lys Gln Pro Arg Val Tyr Thr Ser Tyr Asn Thr Val Gln Asn
                605                 610                 615

Asp Arg Arg Gly Val Glu Lys Met Val Asn Val Val Glu Lys Arg
                620                 625                 630

Pro Thr Gln Lys Ser Leu Asn Gly Asn Leu Leu Val Pro Lys Asn
                635                 640                 645

Ser Ser Ser Ser Asn Val Glu Gly Arg Arg Asp Glu Gln Val Gln
                650                 655                 660

Gly Thr Pro Ser Lys Ala Met Leu Arg Leu Leu Gln Ser Ala Phe
                665                 670                 675
```

FIG. 3D

```
Ser Lys Asn Ala Leu Ser Lys Gln Ser Pro Lys Lys Ser Pro Ser
                680                 685                 690

Ala Lys Leu Ser Ile Pro Tyr Glu Ser Phe Tyr Glu Ala Leu Glu
                695                 700                 705

Lys Leu Asn Lys Pro Ser Lys Leu Glu Gly Ser Glu Asp Ser Leu
                710                 715                 720

Tyr Ser Asp Tyr Val Asp Val Phe Tyr Asn Thr Lys Pro Tyr Lys
                725                 730                 735

His Arg Asp Asp Arg Leu Leu Gln Ala Leu Met Asp Ile Leu Asn
                740                 745                 750

Glu Glu Asn
        753
```

FIG. 4A

```
Met Glu Gly Gly Cys Gly Ser Gln Trp Lys Ala Ala Gly Phe Leu
 1               5                  10                  15

Phe Cys Val Met Val Phe Ala Ser Ala Glu Arg Pro Val Phe Thr
            20                  25                  30

Asn His Phe Leu Val Glu Leu His Lys Asp Gly Glu Glu Glu Ala
        35                  40                  45

Arg Gln Val Ala Ala Glu His Gly Phe Gly Val Arg Lys Leu Pro
    50                  55                  60

Phe Ala Glu Gly Leu Tyr His Phe Tyr His Asn Gly Leu Ala Lys
65                  70                  75

Ala Lys Arg Arg Arg Ser Leu His His Lys Arg Gln Leu Glu Arg
            80                  85                  90

Asp Pro Arg Ile Lys Met Ala Leu Gln Gln Glu Gly Phe Asp Arg
        95                  100                 105

Lys Lys Arg Gly Tyr Arg Asp Ile Asn Glu Ile Asp Ile Asn Met
    110                 115                 120

Asn Asp Pro Leu Phe Thr Lys Gln Trp Tyr Leu Phe Asn Thr Gly
125                 130                 135

Gln Ala Asp Gly Thr Pro Gly Leu Asp Leu Asn Val Ala Glu Ala
            140                 145                 150

Trp Glu Leu Gly Tyr Thr Gly Lys Gly Val Thr Ile Gly Ile Met
        155                 160                 165
```

FIG. 4B

```
Asp Asp Gly Ile Asp Tyr Leu His Pro Asp Leu Ala Tyr Asn Tyr
                170                 175                 180

Asn Ala Asp Ala Ser Tyr Asp Phe Ser Ser Asn Asp Pro Tyr Pro
            185                 190                 195

Tyr Pro Arg Tyr Thr Asp Asp Trp Phe Asn Ser His Gly Thr Arg
        200                 205                 210

Cys Ala Gly Glu Val Ser Ala Ala Ala Ser Asn Asn Ile Cys Gly
    215                 220                 225

Val Gly Val Ala Tyr Asn Ser Lys Val Ala Gly Ile Arg Met Leu
230                 235                 240

Asp Gln Pro Phe Met Thr Asp Ile Ile Glu Ala Ser Ser Ile Ser
245                 250                 255

His Met Pro Gln Leu Ile Asp Ile Tyr Ser Ala Ser Trp Gly Pro
            260                 265                 270

Thr Asp Asn Gly Lys Thr Val Asp Gly Pro Arg Glu Leu Thr Leu
        275                 280                 285

Gln Ala Met Ala Asp Gly Val Asn Lys Gly Arg Gly Gly Lys Gly
    290                 295                 300

Ser Ile Tyr Val Trp Ala Ser Gly Asp Gly Gly Ser Tyr Asp Asp
305                 310                 315

Cys Asn Cys Asp Gly Tyr Ala Ser Ser Met Trp Thr Ile Ser Ile
            320                 325                 330
```

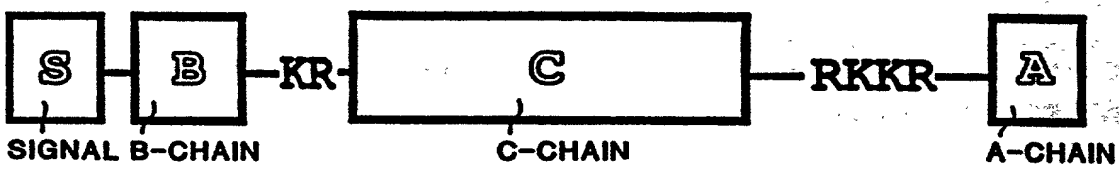
FIG. 4C

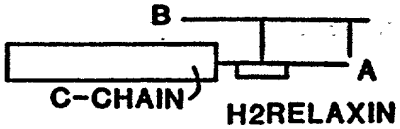
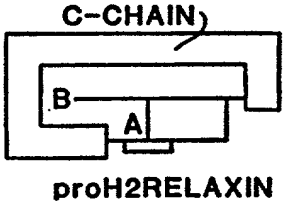
```
Asn Ser Ala Ile Asn Asp Gly Arg Thr Ala Leu Tyr Asp Glu Ser
                335                 340                 345

Cys Ser Ser Thr Leu Ala Ser Thr Phe Ser Asn Gly Arg Lys Arg
                350                 355                 360

Asn Pro Glu Ala Gly Val Ala Thr Thr Asp Leu Tyr Gly Asn Cys
                365                 370                 375

Thr Leu Arg His Ser Gly Thr Ser Ala Ala Ala Pro Glu Ala Ala
                380                 385                 390

Gly Val Phe Ala Leu Ala Leu Glu Ala Asn Leu Asp Leu Thr Trp
                395                 400                 405

Arg Asp Met Gln His Leu Thr Val Leu Thr Ser Lys Arg Asn Gln
                410                 415                 420

Leu His Asp Glu Val His Gln Trp Arg Arg Asn Gly Val Gly Leu
                425                 430                 435

Glu Phe Asn His Leu Phe Gly Tyr Gly Val Leu Asp Ala Gly Ala
                440                 445                 450

Met Val Lys Met Ala Lys Asp Trp Lys Thr Val Pro Glu Arg Phe
                455                 460                 465

His Cys Val Gly Gly Ser Val Gln Asn Pro Glu Lys Ile Pro Pro
                470                 475                 480

Thr Gly Lys Leu Val Leu Thr Leu Lys Thr Asn Ala Cys Glu Gly
                485                 490                 495
```

FIG. 4D

```
Lys Glu Asn Phe Val Arg Tyr Leu Glu His Val Gln Ala Val Ile
500                 505                 510

Thr Val Asn Ala Thr Arg Arg Gly Asp Leu Asn Ile Asn Met Thr
515                 520                 525

Ser Pro Met Gly Thr Lys Ser Ile Leu Leu Ser Arg Arg Pro Arg
530                 535                 540

Asp Asp Asp Ser Lys Val Gly Phe Asp Lys Trp Pro Phe Met Thr
545                 550                 555

Thr His Thr Trp Gly Glu Asp Ala Arg Gly Thr Trp Thr Leu Glu
560                 565                 570

Leu Gly Phe Val Gly Ser Ala Pro Gln Lys Gly Leu Leu Lys Glu
575                 580                 585

Trp Thr Leu Met Leu His Gly Thr Gln Ser Ala Pro Tyr Ile Asp
590                 595                 600

Gln Val Val Arg Asp Tyr Gln Ser Lys Leu Ala Met Ser Lys Lys
605                 610                 615

Gln Glu Leu Glu Glu Glu Leu Asp Glu Ala Val Glu Arg Ser Leu
620                 625                 630

Gln Ser Ile Leu Arg Lys Asn
635     637
```

FIG. 5



Mutant	B/C-Chain	C/A-Chain	Processing
Rx.wt	-KR-↓	-RKKR-↓	
Rx1	-KR-↓	-VKKR-↓	
Rx2	-KR-↓	-RAKR-↓	
Rx3	-KR-↓	-R↓VKAR-	
Rx4	-KR-↓	-RKR↓VA-	
Rx7	-AR-	-RKKR-	
Rx8	-KA-	-RKKR-	